REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following remarks. Claims 1-24 are currently pending in the application with elected claims 14 and 19-24 under active examination. As set forth above, non-elected claims 1-13 and 15-18 have been cancelled.

Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 14 and 19-24 stand rejected under § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time of filing. More particularly, with respect to the claimed methods, the Examiner asserts the following:

> This large genus is represented in the specification by only the particular named SEQ ID No. Thus, applicant has express possession of only one sequence, SEQ ID NO: 1797, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided." (Action, Page 3)

Applicants respectfully traverse this rejection.

Current claim 14 is drawn to a method for determining the presence of a lung cancer in a patient using an oligonucleotide that hybridizes to a sequence set forth in SEQ ID NO:1797. Claim19 is drawn to a method for monitoring the progression of a lung cancer in a patient using an oligonucleotide that hybridizes to a sequence set forth in SEQ ID NO:1797 and comparing the amount of expressed polynucleotide at different time points. Claim 20 is drawn to a method for determining the presence of a lung cancer in a patient using at least two oligonucleotide primers in a reverse transcription polymerase chain reaction, wherein said oligonucleotide primers are effective for amplifying a polynucleotide sequence of SEQ ID NO:1797.

Applicants respectfully submit that the specification more than adequately describes relevant and distinguishing identifying characteristics sufficient to establish that Applicants were in possession of methods employing the genus of polynucleotides currently

claimed. Under the Examination Guidelines set forth by the Patent and Trademark Office, the written description requirement for a claimed genus may be satisfied by the description of a representative number of species or the disclosure of relevant, identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Moreover, satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. (Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099, at 1106).

The instant disclosure provides both relevant identifying characteristics common to the claimed genus of polynucleotides as well as a representative number of species sufficient for the skilled artisan to recognize that Applicants were in possession of the currently claimed methods at the time of filing. The specification, at page 64, lines 15-16, discloses that SEQ ID NO: 1797 is an extended cDNA sequence for clone #24928 (SEQ ID NO: 1339), corresponding to the lung cancer sequence referred to as L978P. The specification further discloses, at page 163, lines 9-26, that SEQ ID NO: 1339 was analyzed by microarray expression analysis and found to be overexpressed by 2-fold or greater in small cell and non-small cell lung tumor probe groups compared to the normal tissue probe group, with the mean expression value for these clones in normal tissues being below 0.1. The specification further discloses, in the table at page 172, that Real Time PCR expression analysis of L978P demonstrated that the sequence was over-expressed 2/2 primary small cell samples, 3/6 small cell lines, 1/1 carcinoid metastases, as well as adeno and squamous tumor pools, with low or no expression detected in normal tissues.

In view of this disclosure, the artisan of ordinary skill would understand, first, that SEQ ID NO: 1797 represents a sequence that is overexpressed in a variety of lung tumor sample types relative to normal tissues, including normal lung tissue, and, accordingly, that SEQ ID NO: 1797 can be used as a probe for detecting the presence of lung cancer in a biological sample, for example by detecting the expression level of SEQ ID NO: 1797 relative to a suitable normal tissue control sample. The skilled artisan would also recognize, in view of this disclosure, that primers can be designed and synthesized, using only routine and art-recognized methodologies,

and that such primers could be readily used for amplifying in a polymerase chain reaction a sequence of SEQ ID NO: 1797, and thereby determining the expression level of SEQ ID NO: 1797 relative to a suitable normal tissue control sample. Further still, the skilled artisan would appreciate, based upon fundamental principles of nucleic acid hybridization, that a multitude of probes, structurally related to SEQ ID NO: 1797, would be capable of specifically hybridizing to an expressed sequence of SEQ ID NO: 1797 and thus would also also useful as diagnostic probes in the same manner and to the same extent that the precise sequence of SEQ ID NO: 1797 is useful as a probe for detecting its own expression. Moreover, guidance with respect to sequences that would be capable of specifically hybridizing to SEQ ID NO: 1797, although certainly provided by the instant specification (e.g., page 150, line 17 to page 151, line 21), is submitted to be unnecessary when such guidance is clearly derivable from what is well known in the art. More particularly, the skilled artisan would readily understand, in light of well established and fundamental principles of nucleic acid hybridization, that sequences structurally related to SEQ ID NO: 1797, and capable of specifically hybridizing to SEQ ID NO: 1797, would be useful in the context of Applicants' claimed methods, despite the fact that they are not identical to the precise sequence of SEQ ID NO: 1797. Indeed, any position that the skilled artisan would reasonably conclude, in view of the instant disclosure, that Applicants were in possession of only the exact sequence of SEQ ID NO: 1797 for use in the presently claimed methods necessarily requires that the skilled artisan also expect that no other sequences, e.g., the primers and probes referenced above, could be predictably and reliably used according to Applicants' disclosure. Applicants respectfully submit that such a position simply belies the current state of the art.

Accordingly, in the context of satisfying the written description requirements under 35 U.S.C. 112, first paragraph, Applicants respectfully submit that a relevant identifying characteristic that the skilled artisan would recognize as common among the genus of polynucleotide sequences encompassed by the instant claims is their ability to be used in detecting expression of SEQ ID NO: 1797, for example using routine probe hybridization and/or PCR-based expression analysis techniques. Moreover, Applicants submit that the disclosure of SEQ ID NO: 1797, in conjunction with its tumor-specific expression profile, provides the

requisite "representative number" of species sufficient to support the instant claims because the skilled artisan, in view of this disclosure, would understand that the Applicants inventive contribution clearly encompasses fragments and primers of SEQ ID NO: 1797, as well as structurally related probes capable of hybridizing to SEQ ID NO: 1797, for use in the currently claimed methods.

Reconsideration of the Examiner's rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 14 and 19-24 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which the invention pertains, or with which it is most nearly connected, to make and use the invention.

First, the Examiner asserts that the instant disclosure does not enable the claimed methods for detection of the many types of lung cancer. The Examiner also asserts that in order to establish efficacy of SEQ ID NO: 1797 as a prognostic marker for cancer requires more than a showing that it is overexpressed in four cell lines. It would allegedly need to be demonstrated in a variety of different cell type models and that this would require "years of inventive effort", with no guarantee of success. The Examiner further asserts that the current specification presents no data to show the relative expression between normal and neoplastic tissue. On this basis the Examiner concludes that the ordinary practitioner would expect significant unpredictability in applying SEQ ID NO: 1797 to detection of any of the many types of lung cancer.

Applicants respectfully traverse this rejection.

Current claim 14 is drawn to a method for determining the presence of a lung cancer in a patient using an oligonucleotide that hybridizes to a sequence set forth in SEQ ID NO:1797. Claim19 is drawn to a method for monitoring the progression of a lung cancer in a patient using an oligonucleotide that hybridizes to a sequence set forth in SEQ ID NO:1797 and comparing the amount of expressed polynucleotide at different time points. Claim 20 is drawn to

a method for determining the presence of a lung cancer in a patient using at least two oligonucleotide primers in a reverse transcription polymerase chain reaction, wherein said oligonucleotide primers are effective for amplifying a polynucleotide sequence of SEQ ID NO:1797.

Contrary to the assertions of the Examiner, the specification as originally filed indeed demonstrates the over-expression of SEQ ID NO: 1797 in a sufficient number of lung tumor types for the skilled artisan to recognize that Applicants had reasonably and adequately enabled the presently claimed methods as of the time of filing. As noted above, the specification, at page 64, lines 15-16, discloses that SEQ ID NO: 1797 is an extended cDNA sequence for clone #24928 (SEQ ID NO: 1339), corresponding to the lung cancer sequence referred to as L978P. The specification further discloses, at page 163, lines 9-26, that SEQ ID NO: 1339 was analyzed by microarray expression analysis and found to be overexpressed by 2-fold or greater in small cell and non-small cell lung tumor probe groups compared to the normal tissue probe group, with the mean expression value for these clones in normal tissues being below 0.1. The specification further discloses, in the table at page 172, that Real Time PCR expression analysis of L978P demonstrated that the sequence was over-expressed 2/2 primary small cell samples, 3/6 small cell lines, 1/1 carcinoid metastases, as well as adeno and squamous tumor pools, with low or no expression detected in normal tissues. Thus, over-expression of SEQ ID NO: 1797 was demonstrated for different lung tumor types (small cell, non-small cell and carcinoid) and for different sample types (primary lung tumors, metastases and lung tumor cell lines) relative to normal tissues. On this basis, an artisan of ordinary skill would understand and expect that SEQ ID NO: 1797 represents a molecular marker not restricted in its use to a single lung tumor sub-type, but capable of detecting lung cancer generally, as currently claimed.

Furthermore, for the convenience of the Examiner, Applicants provide herewith the Declaration of Chaitanya S. Bangur, Ph.D., further confirming what was already described in the specification as filed and now claimed, i.e., that SEQ ID NO: 1797 represents a polynucleotide sequence effective for detecting the presence of lung cancer in a biological sample. More particularly, the Declaration describes the results of Real Time PCR expression analysis of L978 in 87 samples, including sample types comprising primary lung tumors, lung

tumor cell lines and lung pleural effusion samples for lung tumor sub-types comprising small cell carcinoma, atypical carcinoid, adenocarcinoma, squamous cell carcinoma, adeno-squamous mix carcinoma, large cell carcinoma and bronchioalveolar carcinoma. From this analysis, 60/87 samples demonstrated greater than 3-fold over-expression of SEQ ID NO: 1797 relative to normal lung tissue, with 32 of the 60 samples having greater than 10-fold over-expression relative to normal lung tissue.

Thus, in view of the specification as originally filed, and further in view of the enclosed Declaration of Dr. Bangur, Applicants respectfully submit that the presently claimed methods for detecting the presence of lung cancer are indeed fully enabled, and would be recognized as such by the skilled artisan. Reconsideration of this rejection is respectfully requested.

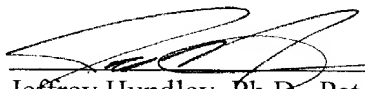
The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Chaitanya S. Bangur et al.

SEED Intellectual Property Law Group PLLC



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Declaration of Chaitanya S. Bangur, Ph.D.,

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